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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,010	08/06/2003	Arthur M. Brown	CHNT-0011P1	7599

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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/635,010	BROWN ET AL.	
	Examiner	Art Unit	
	David A. Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *24-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Amendment of 4/2/04 has been entered. Claims 1-40 are pending. Claims 1-23 and 40 are under examination.

The amendment of 4/2/04 has entered no new matter. The increased breadth of claim 1 is considered to be supported by para. [0036] and [0040]-[0042] of applicant's PG Publication US 2004/0014202. These para. refer to an integral membrane protein in the generic sense.

Applicant's election with traverse of Group I (claims 1-23 and 40) in the reply filed on 4/20/06 is acknowledged. The traversal is on the ground(s) that the search and examination burden would not be undue to examine all claims. This is not found persuasive because firstly, the searches required are different. Applicant's disclosure admits that numerous compositions known in the prior art would be useable in the claimed method of Group II pertaining to treating cardiac arrhythmia. Such prior art would not need to be searched in considering the method of Group I. The position of the Office is that all of the method steps recited in claim 24 of Group II, though they may be in common with those recited in claim 1 of Group I, are steps that merely characterized the inherent properties of a composition. If the composition is already known, as admitted by applicant, the steps add no patentable weight. Secondly, there would be an undue examination burden upon the Office; the method steps of Group II merely characterize the inherent properties of a composition, and they do not define the structural features of the agents identified. As such, applicant was not in possession of the agents identified and not in possession of the method of treating that uses such agents. See Univ. of Rochester... 69 USPQ2d 1886. The consideration of prior art unrelated to the method steps of Claim 1 and the consideration of the 112 description/possession issues relating to the claims of Group II would add a substantial examination burden upon the Office.
The requirement is still deemed proper and is therefore made FINAL.

Claims 1-23 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, step b) and claim 2, step g) "an effective amount" is unclear because there is no statement of what "effect" is to be achieved.

In claim 1, step c) and claim 2, step h) "a sufficient period of time" effective amount" is unclear because there is no statement of what result is to be achieved within this time frame.

In claim 1, step e) and claim 2, step j), the phrase "following incubation with said candidate agent" is unclear because at such point in the method steps no antibody would have be added, such that one could determine "the level of binding of said at least one antibody".

In claim 1 and claim 2, in the "wherein" phrase of each, "relative to control" is unclear because there is no statement of what a "control" does or does not have added thereto as reagents.

In claims 3, 14 and 16, "said first mutant form" lacks antecedent basis in base claim 1. It is suggested that applicant render these claims dependent from claims 2 or 40.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: that there is no indication of what reagent provided in the steps of base claims 1 and 2 provides for the "fluorescence, luminescence, radioactivity, absorbance" to be measured.

In claims 7 and 8, it is not clear whether "said at least one extracellular epitope" refers to that of step d) or that of step i) when one reads theses claims as depending from claim 2.

Claims 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of

elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: that there is no indication of what the "enzyme" of claim 12 does.

Claims 1-23 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In claim 1, step b) and claim 2, step g) applicant has not enabled the adding of "an effective amount of a candidate agent". Applicant has given one no criteria by which to determine what is "an effective amount". Further, if one were to interpret the term "effective" to mean that the amount of agent added is "effective" in altering the level of surface expression of an integral membrane protein, then the claim is circular and would require one of skill to have prophetic knowledge of the amount of candidate reagent that would need to be added in order to obtain such effect, before even conducting any screening/identifying method that would tell one what candidate agents might be effective. Prophetic knowledge is not obtainable by those having an ordinary level of skill in the art.

Claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the case in which the "secondary antibody" is coupled to an enzyme, does not reasonably provide enablement for the case in which the "primary antibody" is coupled to an enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification teaches in para. [0061], [0073]-[0074], and [0103] that the coupling of an enzyme, such as HRP, is to the secondary, not to the primary antibody. In the case of indirect labeling, in which one uses a

primary and a secondary antibody (as in base claim 3), it would be conventional for one to provide the label on the secondary, not on the primary antibody. In the cased of direct labeling (which is not encompassed by base claim 3), it would be conventional to provide the label on the antibody that binds to the extracellular epitope; in such case, no "secondary antibody" is added; since no "secondary antibody" is employed in a direct labeling method, it would be improper to refer to the labeled antibody that binds to the extracellular epitope as a "primary antibody".

Prior to consideration of the prior art, the effective filing date of the instant claims must be established. It is noted that the instant and copending claims of parent application 10/619,184 differ in the order in which steps b)-d) of claim 1 and in which steps g)-i) of claim 2 are recited. The change recited in the instant CIP application is deemed to be supported by the order of steps as shown in Example 1 of the parent and the instant CIP applications. Example 1 is presented in an identical manner in each case. Therefore the instant claims have benefit of the 7/15/03 filing date of parent application 10/619,184.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al (6,034,066) in light of Barclay et al (both cited on Form 892).

Johnson et al conduct experiments in which the expression of the cell surface protein CD23 is monitored; see Barclay et al at page 189 for evidence that CD23 is inherently an integral membrane glycoprotein. Johnson et al show that addition of Der pI to a medium containing CD23+ RPMI 8666 B cells serves to reduce expression of CD23, as determined by binding of monoclonal antibody Bu38, on the surface of these cells. Such reduction is due to the fact that Der pI protein has a proteolytic activity that cleaves the Bu38 epitope from cell surface CD23. In such case the Der pI protein per se may be considered as the instant "candidate agent". In further experiments Johnson et al, test for the effect of candidate proteolytic inhibitors for inhibiting the proteolytic action of Der pI, so that inhibition is determined as a retention of intact CD23 on the cell surface; in such case, the proteolytic inhibitors may be considered as the instant "candidate agent". See Johnson et al at col. 6, line 55-col. 9, line 23 and at Figs 1-3. Claim 1 is thus anticipated.

Claim 4 is rejected since Johnson et al determine binding of the anti-CD23 antibody by means of the fluorescent label FITC; see col. 7, lines 21-25 and 35-39. Claim 7 is rejected since the Bu38 anti-CD23 antibody is assumed to bind to a wild-type epitope, absent teachings of the use of cells with a mutant form thereof.

Claims 1, 3-4, 7 and 12-13 are rejected under 35 U.S.C. 102(b) as being anticipated WOSKA et al in light of Isacke et al (both cited on Form 1449 of 1/10/05).

Woska et al teach screening for compounds which bind to or modify the R7.1 epitope of the CD11a subunit of LFA-1. See paragraph [0002]. The steps disclosed in paragraphs [0011]-[0014], [0017] and [0634-[0637] are consistent with instant claims 1 and 3-4. Claim 7 is rejected, since it is assumed that the

LFA-1 molecules on the cells employed are wild-type, absent teachings of the use of cells with a mutant form thereof. The coupled labels of claims 12-13 are taught in paragraphs [0613]-[0615]. Note that CD11a is an integral, transmembrane cell surface molecule, as shown by Isacke et al (Figure at page 149.

Claim 1, 4 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Vallone et al (2004/0018566, cited on Form 1449 of 1/10/05) in light of Barclay et al (cited on Form 892).

Vallone et al teach screening for compounds which modulate activity of the cell surface protein BIC, which is involved in B-cell activation. As a readout of B-cell activation, Vallone et al teach that one can determine the expression of cell surface proteins such as CD23, CD40L, CD69, CD80 or CD86, all of which increase in level with cell activation. See, for example, paragraphs [0053]-[0057], [0072]-[0078], [0279]-[0284], [0289]-[0290], [0301-[0302], [0316]-[0320]. Note that the expression of such cell surface CD antigens is determined by the binding thereto of fluorescent labeled antibodies and by FACS detection thereof. See, for example [0091], [0095], [0324], and [0327]-[0331]; note para. [0327] teaches use of mammalian cells. Of the CD antigens taught by Vallone et al, at least CD23, CD69, CD80 and CD86 are transmembrane, integral proteins. See Barclay et al at pages 189, 316, 335 and 345 for evidence. Thus instant claims 1 and 4 are anticipated. Claim 7 is rejected, since it is assumed that the CD antigen cell surface molecules on the cells employed are wild-type, absent teachings of the use of cells with mutant forms thereof.

Claim 1, 4-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Qin et al (7,063,953, cited on Form 892).

Qin et al teach screening for compounds that modulate the activity or expression of a β1A sodium channel subunit protein. Among the taught methods of such screening are those that determine effects such as an

increasing of the level of β1A protein expression, a decreasing of the level of β1A protein expression, an increasing of the level of α/β1A complex/protein expression, or a decreasing of the level of α/β1A complex/protein expression. See col. 4, lines 20-44, especially lines 38-42. Note that the β1A sodium channel subunit protein is an integral transmembrane protein (e.g. col. 8, lines1-9). Note screening methods using transformed mammalian cells taught at col. 20, line 13-col. 22, line 2. Note that the methods taught therein for determining the quantity/level of β1A sodium channel subunit protein expression or of α/β1A complex/protein expression include fluorescence activated cell sorting of the protein or complex thereof on the cell surface; see especially col. 21, lines 57-60 and col. 21, line 63-col. 22, line 2. For such a method one would use fluorescent labeled antibodies; Qin et al teach how to make antibodies specific for the β1A channel subunit protein at col. 23, line 50-col. 25, line 40. From the above, instant claims 1 and 4-6 are anticipated. Claim 7 is rejected, since it is assumed that the β1A sodium channel subunit protein cell surface molecules are wild-type, absent teachings of the use of cells with mutant forms thereof in screening assays.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-7 and 12-13 are rejected under 35 U.S.C. 103(a) as being obvious over CURTIS (2003/0022205) in view of WOSKA et al (both cited on Form 1449 of 1/10/05).

Curtis teaches screening for compounds which modulate expression of the cell surface protein 98359. See paragraphs [0242]-[0243] and [0272]. The level of 98359 protein expression can be determined with the use of antibodies by direct or indirect labeling, in accord with instant claims 1 and 3-4; see

paragraph [0319]. Note that the antibodies of Curtis can be directed to an extracellular portion of the 98359 protein and thus bind to the protein on an intact cell which expresses this protein; see paragraph [0201]. Given these teachings of the use of antibodies directed to an extracellular portion of the protein in a direct or indirect labeling method, it would have been obvious to use a conventional method of direct or indirect labeling, analogous to that shown by Woska et al for labeling an extracellular epitope of the LFA-1 protein (e.g. as at paragraphs [0634]-[0637]). Claim 7 is rejected, since it is assumed that the 98359 molecules on the cells employed are wild-type, absent teachings of the use of cells with a mutant form thereof. The coupled labels of claims 12-13 are taught in paragraphs [0613]-[0615] of Woska et al. Note that protein 98359 is an integral, transmembrane cell surface molecule involved in sodium transport, as shown by paragraph [0036] of Curtis; thus instant claims 5-6 and 18 are rejected.

Claims 1, 3-7, 12-13 and 18 are rejected under 35 U.S.C. 103(a) as being obvious over Vallone et al (2004/0018566) in view of WOSKA et al (both cited on Form 1449 of 1/10/05).

Vallone et al teach screening for compounds which modulate expression of the cell surface protein BIC. See paragraphs [0316]-[0319]. The level of BIC protein expression can be determined with the use of antibodies by direct or indirect labeling, in accord with instant claims 1 and 3-4; see paragraph [0382]. Note the teaching therein that the binding of anti-BIC antibodies of Vallone et al can be detected by use of a fluorescence activated cell-sorter (FACS). Note that Woska et al, in their method of labeling an extracellular epitope of the LFA-1 protein, used a flow cytometer to detect membrane bound label; see paragraphs [0019]-[0020] of Woska et al. Since both FACS and flow cytometry involve measuring a fluorescent label on intact cells, it is taken that, in screening for compounds that modulate the expression of BIC, one would be lead to use an antibody directed against an extracellular epitope of BIC, just as

Woska et al used an antibody directed against an extracellular epitope of LFA-1. Given these teachings, it would have been obvious to use a conventional method of direct or indirect labeling, analogous to that shown by Woska et al for labeling an extracellular epitope of the BIC protein. Claim 7 is rejected, since it is assumed that the BIC protein molecules on the cells employed are wild-type, absent teachings of the use of cells with a mutant form thereof. The coupled labels of claims 12-13 are taught in paragraphs [0613]-[0615] of Woska et al. Note that the BIC protein is an integral, transmembrane cell surface molecule involved in cation transport, as shown by paragraphs [0021]-[0024] of Vallone et al; thus instant claims 5-6 are rejected.

Claims 1, 3 and 12-13 are rejected under 35 U.S.C. 103(a) as being obvious over Johnson et al, Vallone et al, or Qin et al, any in view of Martin et al (cited on Form 892).

Each primary reference has been cited supra against instant claim 1 for showing the direct immunofluorescent labeling of a cell surface protein and the detection thereof via FACS/flow cytometry. Martin et al are cited for showing the feature that flow cytometers may be used to detect the immunological staining of cell surface proteins, with the use of an enzyme label. See, for example col. 7, line 63-col. 8, line 64, wherein a primary antibody to a cell surface protein is bound to the cell surface, after which a peroxidase labeled secondary antibody is bound to the primary antibody. Since Martin et al show that such labeling can be detected with a flow cytometer, it would have been obvious to have used an indirect labeling method with an enzyme label, instead of using the direct immunofluorescent labeling method employed in the FACS/flow cytometric methods of any of the primary references.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re

Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-23 and 40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 10/619,184. Although the conflicting claims are not identical, they are not patentably distinct from each other because though the instant and copending claims differ in the order in which steps b)-d) of claim 1 and in which steps g)-i) of claim 2 are recited, it is taken that one of skill would have realized that the order of steps recited in copending claims 1 and 2 should be changed to the order recited in instant claims 1-2. Instant claim 1 is broader in scope than copending claim 1; however, instant claim 1 clearly encompasses what is recited in copending claim 1, when one reads the limits of instant claim 40 into instant claim 1.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Tedder et al (4,987,084) screen for/identify agonists/antagonists of Ca++ ion flux across B-cell membranes mediated by the integral membrane protein CD20. While CD 20 is a known cell surface antigen, Tedder et al do not suggest any screening method in which the level of surface expression is detected with the use of an anti-CD20 antibody. Rather, Tedder et al determine ion flux across the B-cell membrane (e.g. see Col. 3, lines 45+).

Cahalan et al (5,397,702) screen for/identify agonists/antagonists of K+ ion flux across T-cell membranes. They employ methods such asmeasuring current, measuring membrane potential, measuring K+ flux, such as with radioactive tracers, and measuring K+ concentration (e.g. col. 4, lines 56-68 and col. 9, lines 18-27). Though they teach making antibodies to the K+ channel protein (e.g. col. 5, lines 38-41 and col.14, lines 35-58), they teach no use thereof in determining the level of the K+ channel protein in the drug screening assays.

Bram et al (5,969,102) screen for/identify agonists/antagonists of the TACI integral membrane protein, which is involved in Ca++ ion flux across B-cell membranes. Their disclosed screening assays involve, for example, use of a two-hybrid expression system (e.g. col. 7, line 44-col. 8, line 67 and col. 36, lines 54-67 and col. 38, line 28-col. 39, line 3). Though they teach making antibodies to the TACI protein (e.g. col. 6, lines 28-41 and col. 34, line 50-col. 36, line 52), they mention no use thereof in determining the level of the TACI cell surface protein in the drug screening assays.

Huang (6,979,547) teaches a K+ channel blocking protein. An antibody which binds to the external vestibular portion thereof blocks ion transport, as determined by electrophysiological recordings.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
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